

# Diagnostic Use of Radionuclides in Diseases of the Thyroid\*

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Since the introduction of radionuclides into clinical medicine, a number of specific tests have been designed to test thyroid function and to diagnose diseases of the thyroid gland.

These studies can be broadly grouped into *in vivo* and *in vitro* studies. Using  $^{131}\text{I}$  and  $^{125}\text{I}$ , tests have been designed to measure thyroid function at the hypothalamic, pituitary, or thyroid level and at the peripheral level by radioimmunoassay or radioassay of circulating thyroid hormones. The following schema of testing may be used to assess thyroid function:

- I. *Hypothalamus*. Following the intramuscular administration of thyrotropic-releasing hormone, the following changes occur in plasma thyroid-stimulating hormone (TSH) level, which can be measured by radioimmunoassay using  $^{125}\text{I}$ :

CONDITION	TSH
1. Normal	Increased
2. Hyperthyroidism	
A. Toxic Diffuse Goiter	No change
B. Toxic Nodular Goiter	No change
C. Toxic Nodule	No change
3. Hypothyroidism	
A. Hypothalamic	Increased
B. Pituitary	No change
C. Thyroid	Increased

- II. Pituitary capability of secreting TSH under normal and abnormal conditions can be accurately measured by determination of peripheral level of TSH using  $^{125}\text{I}$  radioimmunoassay techniques. The following are TSH values for various thyroid disorders:

CONDITION	TSH
1. Normal	1–10 $\mu\text{U/ml}$ †
2. Hyperthyroidism	
A. Toxic Diffuse Goiter	Normal
B. Toxic Nodular Goiter	Normal
C. Toxic Nodule	Normal
D. Hypothalamic	Increased (1)
E. Pituitary Tumor	Increased (1)
3. Hypothyroidism	
A. Hypothalamic	Low
B. Pituitary	Normal
C. Thyroid	Increased

- III. Assessment of thyroid glandular function can be determined by measuring the concentration of  $^{131}\text{I}$  using basal and dynamic studies following oral administration of  $^{131}\text{I}$ .

1. BASAL STUDIES	PERCENT $^{131}\text{I}$ CONCENTRATION		
	3 hours	5 hours	24 hours
A. Normal Curve	†2.5–11.6%	†4.1–14.9%	†9.0–31.0%
B. Hyperthyroid Curve	>11.6%	14.9%	31.0%
C. Hypothyroid Curve	<2.5	4.1%	9.0%
2. DYNAMIC STUDIES	NORMAL RESPONSE		
A. TSH Stimulation Test	>50% Increase		
B. T-3 Suppression	>50% Decrease		
C. $\text{KClO}_4$ Discharge	< 3% Decrease		

Determination of the circulating thyroid hormones by radioassay and radioimmunoassay techniques using  $^{125}\text{I}$  are readily available and offer accurate measurement of these hormones when properly performed. Normal values for the circulating hormones are as follows:

\* Presented by Dr. Sharpe at the Postgraduate Course in Nuclear Medicine, February 27, 1975, in Williamsburg, Virginia.

† Normal values for the Medical College of Virginia.

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|-------------------------|------------------------------------|
| 1. Total thyroxine      | 5.6–13.1 $\mu\text{g}/\text{dl}$ † |
| 2. Triiodothyronine     | 70–170 $\text{ng}/\text{dl}$ †     |
| 3. Serum free thyroxine | 1.2–3.5 $\text{ng}/\text{dl}$ †    |

**Discussion.** Differential diagnosis of diseases of the thyroid can be made with a high degree of certainty using the previously mentioned tests employing radionuclides. The clinical applicability of the various tests is dependent upon a thorough knowledge of thyroid physiology and interrelationships of trophic hormones and carrier proteins. A review of the disease states and diagnosis using specific tests follows.

1. *Hyperthyroidism.* The vast majority of cases can be diagnosed on clinical grounds alone from the history and physical findings. Confirmation is easily obtained by employing the  $^{131}\text{I}$  uptake at 3, 5, and 24 hours. This will be elevated in the majority of hyperthyroid patients. The above-mentioned test in conjunction with the T-4 and serum free thyroxine (SFT)-4, which are usually elevated, will establish the diagnosis in both Graves' disease and hyperthyroidism due to a nodular goiter. If the diagnosis is suspected on clinical grounds and the above tests are normal, one can then perform the T-3 suppression study. This is done by obtaining a baseline uptake at 3, 5, and 24 hours and then placing the patient on L-triiodothyronine, 150  $\mu\text{g}$  daily for seven days. The uptake in the normal person is suppressed after T-3 administration by at least 50% and is usually below 20% at 24 hours. Hyperthyroid patients seldom suppress below 20% and never below 50% of original uptake. The usual hyperthyroid patient has little or no change in 24-hour uptake following T-3. Data from our laboratory on T-4 and SFT-4 also reveal less than 50% suppression in the hyperthyroid patient with the average change being 1  $\mu\text{g}/\text{dl}$  or less. In rare cases, thyrotoxicosis may be due to elevated T-3 levels. Under these circumstances, the T-4 and SFT-4 and uptake are normal but the latter is nonsuppressible.

2. *Hypothyroidism.* In contrast to hyperthyroidism, hypothyroidism is not always easy to diagnose. This disease has protean manifestations and may be insidious in onset.

Diagnosis when hypothyroidism is suspected clinically is best confirmed by a 24-hour  $^{131}\text{I}$  uptake of less than 9% in 24 hours and a low total and free thyroxine of less than 5.6  $\mu\text{g}/\text{dl}$  and 1.2  $\text{ng}/\text{dl}$ , respectively.

Differentiation between pituitary or thyroid failure can now be made by measuring serum TSH by

$^{125}\text{I}$  radioimmunoassay following intramuscular or intravenous injection of thyrotropin-releasing hormone (TRF). A rise in the serum TSH will occur within approximately 15 to 30 minutes after intravenous injection (2) and 2 to 3 hours after intramuscular TRF (3) injection if the pituitary is intact. Failure to detect a significant rise in TSH after TRF administration implies pituitary failure and hence, establishing the diagnosis of secondary hypothyroidism.

3. *Subacute thyroiditis.* Diagnosis of subacute thyroiditis is usually suggested by the clinical picture of anterior neck pain with exacerbation on swallowing or coughing, radiation of pain to the ears, hoarseness, and signs and symptoms of hypermetabolism. The thyroid is usually enlarged and especially tender.

Laboratory confirmation is established by the presence of a low  $^{131}\text{I}$  uptake at 3, 5, and 24 hours and an elevated T-4 and SFT-4.

4. *Enzymatic defects.* These are usually characterized by the presence of a goiter dating from early childhood or the development of thyroid enlargement following ingestion of certain drugs or foods.

Laboratory studies usually demonstrate an elevated  $^{131}\text{I}$  uptake value, low total T-4 and SFT-4 and discharge of  $^{131}\text{I}$  from the thyroid gland of greater than 3% following oral administration of potassium perchlorate or potassium thiocyanate.

5. *Nodules.* Adequate assessment of both single and multiple nodules in the thyroid gland require that a scan be performed after the administration of  $^{131}\text{I}$  (4),  $^{125}\text{I}$  (5) if available, or  $^{99\text{m}}\text{Tc}$  (6). The former is performed in our laboratory. Evaluation of nonfunctioning nodules subsequently removed surgically at our institution over a ten-year period reveals that single nonfunctioning nodules were malignant in 12.5% of cases, multiple nodules in 16.5%, with the total overall incidence of malignancy being 13.0% in nonfunctioning nodules. (These findings have been noted in a study by J. M. Harrison, MD, R. H. Kirkland, MD, and the author, unpublished data). Or 24 malignant nodules out of 184 nonfunctioning nodules by scan.

The incidence of malignancy in hot nodules in the same study was 1 out of 74, or 1.3%. Reexamination of the scan in the one case revealed that, in retrospect, this most likely was a cold nodule. A functioning nodule is thus strong evidence against malignancy, although some reports of this occurring have appeared in the literature (7).

The autonomous nodule with or without

hyperthyroidism is characterized by uptake in the nodule only and suppression of the remaining thyroid tissue. The nodule fails to suppress following the administration of L-triiodothyronine as previously discussed and there is no significant change in the T-4 or SFT-4 by  $^{125}\text{I}$  radioassay. Thyroid-stimulating hormone and long-acting thyroid stimulator (LATS) values are characteristically low for the former and undetectable for the latter. Autonomy can be confirmed by repeating the scan after administration of 10 units of TSH.

**Conclusion.** Correct assessment of thyroid function and evaluation of nodules can be obtained by the proper application of the appropriate in vivo or in vitro tests as previously discussed. Thyroid function can now be evaluated at the hypothalamic, pituitary, and thyroid level using both  $^{131}\text{I}$  and  $^{125}\text{I}$  and at the peripheral level using  $^{125}\text{I}$  radioassay or radioimmunoassay procedures. Using these procedures as described, quantitative evaluation of thyroid function can be made, and in most instances the disease process can be defined in a specific manner.

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